

This Listing of Claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS

1. *(currently amended)* An isolated, recombinant polypeptide molecule comprising a first amino acid sequence which that is:

- (a) a fragment of a native proteolipid protein (PLP) with the following characteristics:
 - (i) having the sequence of the fragment corresponds to a part of a wild-type PLP sequence or a mutant sequence thereof as compared with the native sequence of said proteolipid protein, and optionally comprising a second amino acid sequence fused in frame thereto to create a fusion polypeptide, which first polypeptide; and
 - (ii) the fragment is encoded by an mRNA having an Internal Ribosome Entry Site ((IRES) wherein at which site translation of the mRNA is initiated initiates at said IRES, such that the N-terminal amino acid residue of said fragment first polypeptide corresponds to an internal residue of said PLP proteolipid protein;
or,
- (b) a fusion polypeptide in which said fragment is a first fusion partner and is fused in frame to a second, fusion partner peptide or polypeptide with a second amino acid sequence.

2. *(currently amended)* The recombinant polypeptide of claim 1 [[or]] wherein the proteolipid protein-PLP is human PLP/DM20.

3. *(currently amended)* The polypeptide or fusion polypeptide of claim 1 selected from the group consisting of:

- (a) PIRP-M, having the amino acid sequence of which is SEQ ID NO:6;
- (b) PIRP-L, having the amino acid sequence of which is SEQ ID NO:8;
- (c) a fusion polypeptide [[of]] between PIRP-M [[(a)]] or PIRP-L [[(b)]] wherein said second amino acid sequence encodes and a naturally fluorescent protein or peptide or polypeptide;
- (d) a His-tagged fusion polypeptide of PIRP-M, having the amino acid sequence of which is SEQ ID NO:12;

- (e) a His-tagged fusion polypeptide of PIRP-L having the amino acid sequence of which is SEQ ID NO:16; and
- (f) PIRP-J, the amino acid sequence of which is a mutant sequence compared to the sequence of said PLP proteolipid protein, the sequence of said PIRP-J being SEQ ID NO:18, or a human homologue of SEQ ID NO:18 thereof.

4. *(currently amended)*: The polypeptide of claim 3 which is PIRP-M having the amino acid sequence of which is SEQ ID NO:6

5. *(withdrawn; currently amended)*: The polypeptide of claim 3 which is PIRP-L, having the amino acid sequence of which is SEQ ID NO:8.

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7. *(currently amended)* The fusion polypeptide of claim 3 wherein said fluorescent polypeptide protein is yellow or green fluorescent protein (GFP) or a fluorescent homologue thereof.

8. *(currently amended)*: The His-tagged PIRP-M fusion polypeptide of claim 3 having the sequence of which is SEQ ID NO:12.

9. *(withdrawn; currently amended)* The His-tagged PIRP-L fusion polypeptide of claim 3 having the sequence of which SEQ ID NO:16.

10. *(withdrawn; currently amended)* An isolated nucleic acid encoding

- (A) the PLP fragment polypeptide of claim 1 the sequence of which polypeptide corresponds to said wild-type PLP or to the mutant sequence thereof, or
- (B) the fusion polypeptide.

11. *(withdrawn)*: The nucleic acid of claim 10 which is a DNA molecule.

12. *(withdrawn)*: The nucleic acid of claim 10 which is an RNA molecule.

13. *(withdrawn; currently amended)* The nucleic acid of claim 10 wherein the PLP proteolipid protein of which the polypeptide is a fragment is human PLP/DM20.

14. *(withdrawn; currently amended)* The nucleic acid of claim 10 that encodes encoding a polypeptide or fusion polypeptide selected from the group consisting of:

- (a) PIRP-M, having the amino acid sequence of which is SEQ ID NO:6;
- (b) PIRP-L, having the amino acid sequence of which is SEQ ID NO:8;
- (c) a fusion polypeptide of PIRP-M [[(a)] or PRIP-L [[(b)]] wherein said second amino-acid sequence encodes a peptide or polypeptide is naturally fluorescent protein or peptide;
- (d) a His-tagged fusion polypeptide of PIRP-M having the amino acid sequence of which is SEQ ID NO:12;
- (e) a His-tagged fusion polypeptide of PIRP-L having the amino acid sequence of which is SEQ ID NO:16; and
- (f) PIRP-J, the sequence of which is a having a mutant sequence compared to said PLP proteolipid protein, the sequence of said PIRP-J being SEQ ID NO:18, or a human homologue thereof.

15. *(withdrawn)* The nucleic acid of claim 14 which encodes PIRP-M and has a nucleotide sequence SEQ ID NO:5 or SEQ ID NO:9.

16. *(withdrawn)* The nucleic acid of claim 14 which encodes PIRP-L and has a nucleotide sequence SEQ ID NO:7 or SEQ ID NO:13.

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18. *(withdrawn)* The nucleic acid of claim 14 which encodes said His-tagged fusion polypeptide of PIRP-M, which nucleic acid has a nucleotide sequence SEQ ID NO:11;

19. *(withdrawn)* The nucleic acid of claim 14 which encodes said His-tagged fusion polypeptide of PIRP-L, which nucleic acid has a nucleotide sequence SEQ ID NO:15;

20. *(withdrawn; currently amended)* The nucleic acid of claim 14 which encodes said fusion polypeptide wherein said second peptide or polypeptide is amino-acid sequence encodes a naturally fluorescent protein or peptide.

21. *(withdrawn; currently amended)* The nucleic acid of claim 20 wherein said fluorescent polypeptide protein is yellow or green fluorescent protein (GFP) or a fluorescent homologue thereof.

22. *(withdrawn):* The nucleic acid of claim 10 operatively linked to a promoter.

23. *(withdrawn):* The nucleic acid of claim 22 , wherein the promoter is one which is expressed in a mammalian cell.

24. *(withdrawn)*: The nucleic acid of claim 23 wherein said mammalian cell is a neuronal cell, a glial cell or a stem cell.
25. *(withdrawn)*: The nucleic acid of claim 24 wherein said glial cell is an oligodendrocyte.
26. *(withdrawn)*: The nucleic acid of claim 24 wherein the stem cell is a neural stem cell, an oligodendrocyte progenitor cell, an embryonic stem cell or a hemopoietic stem cell.
27. *(withdrawn)*: A vector comprising the nucleic acid of claim 10.
28. *(withdrawn)*: The vector of claim 27, selected from the group consisting of PLP-GFP/DM20-GFP; PLP-GFP/DM20-GFP Tet-On; PLP-GFP/DM20-GFP M1L; PLP-GFP/DM20-GFP M1L/M205L; PLP-GFP/DM20-GFP M1L/M234L; PLP-GFP/DM20-GFP M1L/M205L/M234L; PLP-GFP/DM20-GFP Pro-; JPLP-GFP/JDM20-GFP; JPLP-GFP/JDM20-GFP M1L; JPLP-GFP/JDM20-GFP M1L/M205L; RshPLP-GFP/RshDM20-GFP M1L; PLP-GFP/DM20-GFP M1L/K268R; PLP-GFP/DM20-GFP M1L/K275R; PLP-GFP/DM20-GFP M1L/K268R/K275R; and PLP-GFP/DM20-GFP M1L/R272K
29. *(withdrawn)*: An expression vector or cassette comprising the nucleic acid of claim 10 operatively linked to
 - (a) a promoter; and
 - (b) optionally, additional regulatory sequences that regulate expression of said nucleic acid in a eukaryotic cell.
30. *(withdrawn)*: The expression vector or cassette of claim 27 comprising a vector selected from the group consisting of pCMV; pEGFP-N1; pEYFP-N1; pEGFP-Tet-On; pBluescript II KS+; and pET-14b.
31. *(withdrawn; currently amended)*: The expression vector or cassette of claim 27_[28] selected from the group consisting of 205M-CMV/234M-CMV; 205M-His-CMV/234M-His-CMV; 205M-BsKS+/234M-BsKS+; 205M-His-BsKS+/234M-His-BsKS+; and 205M-ET-14b/234M-ET-14b.
32. *(withdrawn)*: A cell which has been modified to comprise the nucleic acid of claim 10.
33. *(withdrawn)*: The cell of claim 32 which is a mammalian cell.
34. *(withdrawn)*: A cell which has been modified to comprise the vector of claim 27.
35. *(withdrawn)*: A cell which has been modified to comprise the vector or expression cassette of claim 31.
36. *(withdrawn)*: The cell of claim 35 which expresses said nucleic acid.

37. *(withdrawn)*: The cell of claim 36 which is mammalian cell.
38. *(withdrawn)*: The cell of claim 37 wherein said mammalian cell is a neuronal cell, a glial cell or a stem cell.
39. *(withdrawn)*: The cell of claim 38 wherein said glial cell is an oligodendrocyte.
40. *(withdrawn)*: The cells of claim 38 wherein the stem cell is a neural stem cell, an oligodendrocyte progenitor cell, an embryonic stem cell or a hemopoietic stem cell.
41. *(previously presented)* A pharmaceutical composition, comprising:
(a) pharmaceutically acceptable excipient in combination with
(b) the polypeptide of claim 1.
42. *(withdrawn)*: A pharmaceutical composition, comprising:
(a) pharmaceutically acceptable excipient in combination with
(b) the nucleic acid of claim 23.
43. *(withdrawn; currently amended)* A pharmaceutical composition, comprising:
(a) pharmaceutically acceptable excipient in combination with
(b) the expression vector or cassette of claim 29.[:]
44. *(withdrawn)*: A pharmaceutical composition, comprising:
(a) pharmaceutically acceptable excipient in combination with
(b) the cell of claim 33.
45. ***PREVIOUSLY CANCELED***
46. *(withdrawn)*: A method for stimulating oligodendroglial cells or Schwann cells and promoting remyelination, comprising providing to said cells an effective amount of the polypeptide of claim 4 or a functional derivative thereof, thereby stimulating said cells and promoting remyelination.
47. *(withdrawn)*: The method of claim 46 that is carried out *in vivo* in a mammalian subject in need of remyelination.
48. *(withdrawn)*: A method of treating a demyelinating or dysmyelinating disease or disorder in a mammalian subject, comprising administering to said subject
(i) the polypeptide of claim 4 or a functional derivative thereof, or
(ii) a pharmaceutical composition comprising said polypeptide or functional derivative,

thereby treating said disease or disorder.

49. *(withdrawn)*: The method of claim 48, wherein the disease or disorder is multiple sclerosis, closed head trauma associated with Parkinson's-like symptoms, hypoxic ischemia, or spinal cord trauma.

50. *(withdrawn)*: A method for stimulating oligodendroglial cells or Schwann cells and promoting remyelination in a subject, comprising administering to a subject in need of remyelination an effective amount of the cells of claim 32 which have been modified by said nucleic acid that

- (i) has a nucleotide sequence SEQ ID NO:5 or SEQ ID NO:9; or
- (ii) encodes a polypeptide having the amino acid sequence SEQ ID NO:6,

thereby promoting said remyelination.

51. *(withdrawn; currently amended)*: A method of treating a demyelinating or dysmyelinating disease or disorder in a mammalian subject, comprising administering to said subject the cells of claim 32 which have been modified by said nucleic acid that

- (i) has a nucleotide sequence SEQ ID NO:7 [[5]] or SEQ ID NO: 13[[9]]; or
- (ii) encodes a polypeptide having the amino acid sequence SEQ ID NO:8[[6]],

thereby treating said disease or disorder.

52. *(withdrawn)*: A method of stimulating neural stem cell survival and promoting differentiation or maturation of said cells along the oligodendrocyte pathway, comprising providing to said neural stem cells an effective amount of the polypeptide of claim 4 or a functional derivative thereof.

53. *(withdrawn)*: A method for stimulating proliferation of oligodendrocytes and/or oligodendrocyte precursors, comprising providing to said oligodendrocytes and/or precursors an effective amount of the polypeptide of claim 4 or a functional derivative thereof.

54. *(withdrawn)*: A method of protecting oligodendrocytes from apoptotic death comprising providing to oligodendrocytes an effective amount of the polypeptide of claim 4 or a functional derivative thereof.

55. *(withdrawn)*: A method for treating a disease or disorder in which one or more of oligodendrocytic (a) differentiation, (b) maturation, (c) proliferation, and (d) inhibition of cell death is palliative or curative for said disease or disorder, comprising administering to a subject in need of such treatment an effective amount of

- (i) the polypeptide of claim 4 or a functional derivative thereof, or
- (ii) a pharmaceutical composition comprising said polypeptide or functional derivative,

thereby treating said disease or disorder.

56. (*withdrawn*): A method for treating a disease or disorder in which one or more of oligodendrocytic (a) differentiation, (b) maturation, (c) proliferation, and (d) inhibition of cell death is palliative or curative for said disease or disorder, comprising administering to a subject in need of such treatment an effective amount of the cells of claim 32 which have been modified by said nucleic acid that

- (i) has a nucleotide sequence SEQ ID NO:5 or SEQ ID NO:9; or
- (ii) encodes a polypeptide having the amino acid sequence SEQ ID NO:6,

thereby treating said disease or disorder.

57. (*withdrawn*): A method for regulating or inhibiting the production or action of PLP/DM20 or of PIRP-M polypeptide under conditions in which said PLP/DM20 or PIRP-M is pathogenically produced in cells or in a subject, comprising providing to the cells or to the subject an effective amount of the polypeptide of claim 5 or a functional derivative thereof.

58. (*withdrawn*): The method of claim 57 wherein the polypeptide or functional derivative is administered to a subject with oligodendrogloma or a benign glial tumor

59. (*withdrawn*): A method for regulating or inhibiting the production or action of PLP/DM20 or of PIRP-M polypeptide under conditions in which said PLP/DM20 or PIRP-M is pathogenically produced in cells or in a subject, comprising providing to the cells or to the subject an effective amount of the cells of claim 32 which have been modified by said nucleic acid that

- (i) has a nucleotide sequence SEQ ID NO:7 or SEQ ID NO:13, or
- (ii) encodes a polypeptide comprising an amino acid sequence SEQ ID NO:8.

60. (*withdrawn*): The method of claim 59 wherein the cells being provided are administered to a subject with oligodendrogloma or a benign glial tumor.